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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,695	11/21/2003	Leong Ng	ISA-012.01	1345

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
12/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,695	NG, LEONG	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,16 and 22-30* is/are pending in the application.

4a) Of the above claim(s) *11-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 16 and 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/17/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response filed on 08/17/2009 is acknowledged.

2. Claims 1-7, 16 and 22-30 are pending.

3. Claims 22-25 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 08/14/2006.

4. Claims 1-7, 16 and 26-30 are currently under examination as they read on a method for detectingan increased risk of heart disease.

5. Applicant's IDS document filed on 08/17/2009 is acknowledged.

6. The following rejections are necessitated by the amendment filed on 08/17/2009.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-5, 7, 16 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsukamoto et al. (IDS document filed on 06/29/2004; Reference AZ) in view of Karl et al. (IDS document filed on 06/16/2004; Reference AJ) and Coligan et al. (PTO-892; Reference U).

Tsukamoto et al. teaches a method for determining atherosclerosis in a human subject, comprising (a) contacting atherosclerotic aorta samples with a monoclonal antibody specific for a instant SEQ ID NO: 2 with two additional amino acids added onto the C-terminus of ORP150 in order to detect the level of ORP150 in the aorta sample, and (b) comparing the level of ORP 150 in the atherosclerotic aorta sample with the level of ORP 150 that is indicative of the absence of heart disease, the level of ORP 150 that is indicative of the absence of heart disease being the level of ORP150 from humans free from heart disease (control non-atherosclerotic patient aorta samples); and wherein the method comprises an immunoassay (In particular, paragraph spanning pages 1931-32; paragraph spanning columns on page 1935, whole document). The reference also teaches that atherosclerosis patients have endogenous anti-ORP150 antibody in their serum as measured by ELISA (In particular, page 1932, right column second full paragraph; page 1937 to the 'Discussion' section, whole document).

The claimed invention differs from the prior art in the recitation of detecting ORP150 "with an antibody specific for amino acids sequence LAVMSVDLGSESM" in claim 1; "in a bodily fluid sample" of claim 1; "wherein the bodily fluid sample is plasma" of claim 3; "wherein the immunoassay is a lateral flow immunoassay" of claim 5; "wherein the immunoassay is a flow through immunoassay of claim 6; "wherein the level of ORP150 is monitored periodically" of claim 16; "further comprising measuring the level in the bodily fluid sample of a second marker indicative of heart disease" of claim 26; "wherein the second marker is a natriuretic peptide" of

claim 27; "wherein the level of the second marker is compared with a level of the second marker which is indicative of the absence of heart disease" of claim 28; "wherein the level of the natriuretic peptide is compared with the level of the natriuretic peptide that is indicative of the absence of heart disease is the level of the natriuretic peptide from one ore more mammalian subjects free from heart disease, or a previously determined reference range for the natriuretic peptide in mammalian subjects free from heart disease" of claim 29; and "wherein the level of the second marker is measured by contacting the sample with an antibody specific for the second marker in order to detect the level of the second marker in the bodily fluid sample" of claim 30.

Coligan et al. teaches selection of a 10-15 amino acid peptide sequence from a protein's N-terminus to generate antibodies that will bind to native antigen because the N-terminus of a protein is often exposed in the native protein (In particular, page 5.6., third paragraph and 'Seelection of an N-terminal peptide' section on pages page 5.6.2-5.6.3).

Karl et al. teaches immunoassay reagents and methods for measurement of natriuretic peptides in blood and plasma for diagnosis of cardiac disease (In particular, abstract, introduction, and page 180, last paragraph). The reference teaches using a sandwich assay, which is a lateral flow immunoassay as defined in the instant specification, to detect natriuretic peptide NT-proBNP to monitor cardiac disease and therapy. Karl et al teaches that sandwich format immunoassays, are efficient "highly sensitive" and "specific" (In particular, page 177, abstract).

It would have been obvious to use antibodies that bind to peptides consisting of the first 10-15 amino acids of the ORP150 protein because Coligan et al teaches that 10-15 amino acid

peptides from the N-terminus of proteins are used to generate antibodies to the native protein because the N-terminus is often exposed in the native protein. Tsukamoto et al generated antibodies to the first 15 amino acid residues of the ORP150 protein which bind to native ORP150, therefore one would have a high expectation of success in generating antibodies to the N-terminal 13 amino acids of ORP150 which also bind to native ORP150 protein and which would be equally effective in detecting ORP150 in aorta samples.

It would have been obvious to one of ordinary skill in the art at the time of invention to detect ORP150 in the plasma because bodily fluids such as blood, serum and plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for performing an immunoassay. In addition, Tsukamoto et al specifically teaches that atherosclerosis patients have ORP150 in aortic samples and endogenous anti-ORP150 antibody in their plasma, so it would be obvious to measure ORP150 in bodily fluids such as plasma and serum, particularly because of the convenience in obtaining blood, serum and plasma samples.

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150 protein in a patient's aorta sample with detection of ORP 150 in a bodily fluid sample such as plasma in a lateral flow immunoassay and to compare the amount to a healthy control to detect increased risk of heart disease and to monitor disease periodically because, as taught by Karl et al., sandwich format immunoassays, are efficient " highly sensitive" and "specific" (In particular, page 177, abstract) and because bodily fluids such

as plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for performing such an assay.

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of natriuretic peptide second markers in a patient's bodily fluid, such as plasma, using antibodies to the natriuretic peptide second markers with detection of ORP150 in a lateral flow immunoassay to detect increased risk heart disease. Lateral flow immunoassays, such as sandwich format immunoassays, are efficient "highly sensitive" and "specific" (In particular, page 177, abstract). Bodily fluids such as plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for performing such an assay.

It would be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150 and BNP or N-BNP natriuretic peptides with a lateral flow immunoassay because it is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. Claims 1-5, 7, 16 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsukamoto et al. (IDS document filed on 06/29/2004; Reference AZ) in view of Coligan et al. (PTO-892; Reference U) and Hall et al. (IDS filed on 6/18/2004, Reference AG).

Tsukamoto et al. has been discussed supra.

The claimed invention differs from the prior art in the recitation of detecting ORP150 "with an antibody specific for amino acids sequence LAVMSVDLGSESM" in claim 1; "in a bodily fluid sample" of claim 1; "wherein the bodily fluid sample is plasma" of claim 3; "wherein the immunoassay is a lateral flow immunoassay" of claim 5; "wherein the immunoassay is a flow through immunoassay of claim 6; "wherein the level of ORP150 is monitored periodically" of claim 16; "further comprising measuring the level in the bodily fluid sample of a second marker indicative of heart disease" of claim 26; "wherein the second marker is a natriuretic peptide" of claim 27; "wherein the level of the second marker is compared with a level of the second marker which is indicative of the absence of heart disease" of claim 28; "wherein the level of the natriuretic peptide is compared with the level of the natriuretic peptide that is indicative of the absence of heart disease is the level of the natriuretic peptide from one ore more mammalian subjects free from heart disease, or a previously determined reference range for the natriuretic peptide in mammalian subjects free from heart disease" of claim 29; and "wherein the level of

the second marker is measured by contacting the sample with an antibody specific for the second marker in order to detect the level of the second marker in the bodily fluid sample" of claim 30.

Coligan et al. has been discussed supra.

Hall et al. teaches detection of natriuretic peptide, particularly N-terminal pro-brain natriuretic peptide and brain natriuretic peptide, in the diagnosis, management and periodic monitoring of heart failure patients by comparing the amounts to healthy control patients. The reference teaches that the determinations should be combined with other diagnostic examinations, including other peptide determinations to improve diagnostic performance and that it can be done over a series of time points to better monitor disease (In particular, page 395, fourth paragraph, page 396, fourth paragraph and page 397, last paragraph). The reference also teaches the ease of detecting the proteins in a patient's plasma (In particular, page 395, third paragraph and page 396, first and last paragraphs) and detection by immunoassay (In particular, pages 395, second paragraph).

It would have been obvious to use antibodies that bind to peptides consisting of the first 10-15 amino acids of the ORP150 protein because Coligan et al teaches that 10-15 amino acid peptides from the N-terminus of proteins are used to generate antibodies to the native protein because the N-terminus is often exposed in the native protein. Tsukamoto et al generated antibodies to the first 15 amino acid residues of the ORP150 protein which bind to native ORP150, therefore one would have a high expectation of success in generating antibodies to the N-terminal 13 amino acids of ORP150 which also bind to native ORP150 protein and which would be equally effective in detecting ORP150 in aorta samples.

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine the determination of ORP 150 with the determinations of other diagnostic markers, such as natriuretic peptides, for diagnosis of heart failure in view of the suggestion in Hall et al. to combine tests to improve diagnostic performance. It would also be obvious to one of ordinary skill in the art at the time the invention was made to detect the level of ORP 150 alone or in combination with a second marker to better adjust a patient's therapy according to their cardiac disease and severity associated peptide levels, as suggested by Hall et al. (In particular, page 396, third paragraph and page 396, second paragraph). It is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tsukamoto et al. (IDS document filed on 06/29/2004; Reference AZ) in view of Coligan et al. (PT-892; Reference

U) and Hall et al. (IDS filed on 6/18/2004, Reference AG) as applied to claims 1-5, 7 and 26-30 above and further in view of May et al. (PTO-892 mailed on 07/11/2007; Reference A).

Tsukamoto et al., Coligan et al and Hall et al. have been discussed supra.

The claimed invention differs from the prior art in the recitation of "wherein the immunoassay is a flow-through immunoassay" of claim 6.

May et al. teaches a specific, flow-through immunoassay for determining pregnancy that reacts a liquid biological sample with a test strip made of dry porous material that absorbs the liquid biological sample and transports the biological sample to a membrane zone with immobilized antibody to hCG. If the antigen is present in a biological sample, a colored spot develops on the surface of the membrane through use of a color tagged secondary antibody. (In particular, Claims 1-34 and column 2 lines 3-20).

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150 protein in a patient's bodily fluid, such as plasma, using monoclonal antibodies to the ORP 150 protein in a flow-thorough immunoassay to detect increased risk of heart disease. The May et al. reference teaches that such a device is optimal as it is specific, reliable, quick, convenient, commercially available and suitable for home-use because of the lack of requisite skill and ease of obtaining a bodily fluid sample for use (In particular column 1 lines 10-45 and lines 64-67 and column 2, lines 1-2). Bodily fluids such as plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for performing such an assay.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tsukamoto et al. (IDS document filed on 06/29/2004; Reference AZ) in view of Coligan et al. (PT-892; Reference U) and Karl et al. (IDS document filed on 06/16/2004; Reference AJ) as applied to claims 1-5, 7 and 26-30 above and further in view of May et al. (PTO-892 mailed on 07/11/2007; Reference A).

Tsukamoto et al., Coligan et al and Karl et al. have been discussed supra.

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It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150 protein in a patient's bodily fluid, such as plasma, using monoclonal antibodies to the ORP 150 protein in a flow-thorough immunoassay to detect increased risk of heart disease. The May et al. reference teaches that such a device is optimal as it is specific, reliable, quick, convenient, commercially available and suitable for home-use because of the lack of requisite skill and ease of obtaining a bodily fluid sample for use (In particular column 1 lines 10-45 and lines 64-67 and column 2, lines 1-2). Bodily fluids such as plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for performing such an assay.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

December 4, 2009
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/Maher M. Haddad/
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